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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/598,982	06/21/2000	Mark Maffitt	34506.104	6761

7590 06/20/2005

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EXAMINER

RAMIREZ, DELIA M

ART UNIT PAPER NUMBER

1652

DATE MAILED: 06/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

**Advisory Action  
Before the Filing of an Appeal Brief**

<b>Application No.</b> 09/598,982	<b>Applicant(s)</b> MAFFITT ET AL.	
<b>Examiner</b> Delia M. Ramirez	<b>Art Unit</b> 1652	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 23 May 2005 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1.  The reply was filed after a final rejection, but prior to filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a)  The period for reply expires 3 months from the mailing date of the final rejection.  
b)  The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2.  The reply was filed after the date of filing a Notice of Appeal, but prior to the date of filing an appeal brief. The Notice of Appeal was filed on \_\_\_\_\_. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3.  The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because  
(a)  They raise new issues that would require further consideration and/or search (see NOTE below);  
(b)  They raise the issue of new matter (see NOTE below);  
(c)  They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or  
(d)  They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: \_\_\_\_\_. (See 37 CFR 1.116 and 41.33(a)).

4.  The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).

5.  Applicant's reply has overcome the following rejection(s): \_\_\_\_\_.

6.  Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

7.  For purposes of appeal, the proposed amendment(s): a)  will not be entered, or b)  will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: 1-6,9-12,17-25,34-36 and 43-45.

Claim(s) objected to: none.

Claim(s) rejected: 13-16,37,41 and 42.

Claim(s) withdrawn from consideration: none.

AFFIDAVIT OR OTHER EVIDENCE

8.  The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).

9.  The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing of good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).

10.  The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11.  The request for reconsideration has been considered but does NOT place the application in condition for allowance because: \_\_\_\_\_.

12.  Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s). \_\_\_\_\_

13.  Other: see attached.

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**ADVISORY ACTION**

1. Claims 1-25, 34-37, 41-45, 54-58 are pending.
2. The request for amending claims 1, 7-8, 19-20, and arguments filed on 5/23/2005 under 37 CFR 1.116 in reply to the Final Action mailed on 3/24/2005 are acknowledged. The proposed amendments to the claims has been considered and they will be entered. While the proposed amendments to the claims are deemed sufficient to overcome some of the grounds of rejection under 35 USC 112, second paragraph, the amendments are not deemed sufficient to overcome all the 35 USC first and second paragraph rejections previously applied for the reasons set forth below.
3. It is noted that while Applicants have indicated in the Remarks section of the response filed on 5/23/2005 that a substitute Figure 1 has been submitted, the Examiner is unable to locate such Figure in the file. Thus, the objection to the specification previously applied is maintained for the reasons of record.
4. Claims 7-8 would remain rejected under 35 USC 112, second paragraph due to the recitation of "DNA sequence encoding a proteolytic tryptase as shown in Fig. 1 having an active site mutation at an amino acid position selected from positions 44, 91, and 194, wherein the DNA sequence encoding the proteolytic tryptase ....selected from the group consisting of SEQ ID NO: 20, SEQ ID NO: 22,....." for the reasons of record. As previously indicated in the Final Action mailed on 3/24/2005, the polypeptides of SEQ ID NO: 21, 23, 25, 27, 37, 39, 41 and 43 do not appear to correspond to the proteolytic tryptase of Fig. 1 (SEQ ID NO: 52) having an active site mutation at the positions recited since the polypeptides of SEQ ID NO: 21, 23, 25, 27, 37, 39, 41 and 43 are 249 amino acid long, lack the first 30 amino acids of the proteolytic tryptase shown in Fig. 1 (SEQ ID NO: 52), and contain 4 amino acids (LEKR) prior to the mature fragment which are not present in the proteolytic tryptase of Fig. 1. Therefore, a DNA encoding the polypeptides of SEQ ID NO: 21, 23, 25, 27, 37, 39, 41 and 43 is not a DNA encoding the proteolytic tryptase of Fig. 1 (SEQ ID NO: 52) with active site mutations at positions 44, 91, or 194. It is suggested

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that claims 7-8 be amended such that the term reads "DNA sequence encoding a proteolytic trypsin, wherein the DNA sequence encoding the proteolytic trypsin ...selected from the group consisting of SEQ ID NO: 20, SEQ ID NO: 22,.....". For examination purposes, the term "as shown in Fig. 1 having an active site mutation at an amino acid position selected from positions 44, 91, and 194" will not be given any patentable weight. Correction is required.

5. Claims 13-16, 37, 41-42 would remain rejected under 35 USC 112, first paragraph as lacking written description and enablement for the reasons of record. Applicants argue that the claims are adequately described and enabled because the specification clearly exemplifies proteolytic trypsinases having mutations in the active site and enables how to make such mutations. Applicants also submit that Applicant's position in regard to the description of the genus of trypsinases recited is supported by the knowledge in the art that trypsinases are tetrameric enzymes. Applicants also refer to the sequences disclosed in the sequence listing, list of suitable promoters and Table 1 disclosed in the specification, in support of the argument that the genus of trypsinases recited is adequately described.

6. Applicant's arguments have been fully considered but are not deemed persuasive to overcome the instant rejections. As previously indicated, the genus of trypsinases required is a large and structurally variable genus. There is no disclosure of a structure/function correlation which would adequately describe all trypsinases as recited. Furthermore, there is no disclosure of the structural elements required in any trypsinase or which are the structural elements of known trypsinases which are required in any trypsinase. It is reiterated herein that while a sufficient description of a genus of DNAs may be achieved by a recitation of a representative number of polynucleotides defined by their nucleic acid sequence or a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus, in the instant case, there is no structural feature recited in the instant claims. The Examiner acknowledges that the sequence listing and the DNA sequences provided in the specification. However, those sequences do not correspond to polynucleotides encoding several trypsinases of diverse origin but

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rather to polynucleotides encoding several mutated forms of the same tryptase. In addition, while it is agreed that known tryptases are tetrameric enzymes, it is unclear as to how this characteristic of known tryptases can provide adequate description of the structure of all tryptases (known and unknown) as encompassed by the claims. In regard to the scope of the enablement rejection, as previously indicated, in view of the lack of information as to the structures of all the tryptases recited in the claims, or a correlation between structure/function, it would require undue experimentation to isolate/make all the tryptases required in the claimed invention. Thus, for the reasons of record and those set forth above, the claimed invention is neither adequately described nor fully enabled by the teachings of the specification.

7. For purposes of Appeal, the status of the claims is as follows:

Claim(s) allowed: 1-6, 9-12, 17-25, 34-36, 43-45

Claims(s) objected to: NONE

Claim(s) rejected: 13-16, 37, 41-42

Claim(s) withdrawn from consideration: NONE

8. Certain papers related to this application may be submitted to Art Unit 1652 by facsimile transmission. The FAX number is (571) 273-8300. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If Applicant submits a paper by FAX, the original copy should be retained by Applicant or Applicant's representative. **NO DUPLICATE COPIES SHOULD BE SUBMITTED**, so as to avoid the processing of duplicate papers in the Office.

9. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PMR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should

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you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Delia M. Ramirez whose telephone number is (571) 272-0938. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy can be reached on (571) 272-0928. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Delia M. Ramirez, Ph.D.  
Patent Examiner  
Art Unit 1652

DR  
June 13, 2005

  
REBECCA E. PROITY  
PRIMARY EXAMINER  
GROUP ~~1800~~  
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